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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,000	01/08/2007	Xiaobing Wu	ZLO.102	8805

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
02/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

Office Action Summary	Application No.	Applicant(s)	
	10/576,000	WU ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Zachariah Lucas in Art Unit 1648.

2. Claims 1-3 are pending and under consideration in the application.

3. In the prior action, mailed on September 29, 2009, claims 1-4, 6-8, 10, and 11 were pending; with claims 4, 6-8, 10, and 11 withdrawn from consideration; and claims 1-3 under consideration and rejected.

4. In the Response of December 28, 2009, the Applicant cancelled withdrawn claims 4, 6-8, 10, and 11; and amended claims 1-3.

5. This action is made Non-Final in view of the new rejections presented below.

Specification

6. **(New Objection)** The disclosure is objected to because of the following informalities: in numerous instances throughout the specification, boxes have been substituted for various other characters.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. **(Prior Rejection- Withdrawn)** Claim 2 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite due to the reference in the claim to "the XbaI site." Applicant's arguments in traversal are found persuasive. The rejection is therefore withdrawn.

9. **(New Rejection)** Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on recombinant HSV-1 particles comprising a heterologous sequence "represented by" SEQ ID NO: 1. It is not clear what is meant by the quoted language. It is not clear if the "represented by" phrase requires the presence of SEQ ID NO: 1 specifically, or if the indicated language permits some variation from SEQ ID NO: 1- in which case it is not clear what the extent of such variation may be.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. **(Prior Rejection- Withdrawn)** Claims 1-3 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement with respect to the genus of nonessential gene regions of any HSV virus. The claims have been amended to refer to nonessential gene regions of HSV-1. Upon consideration of the Applicant's arguments, and the teachings of the art (such as the identification of several nonessential genes on pages 2-3 of U.S. 20020028925), the rejection is withdrawn.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. **(New Rejection)** Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Conway et al. (J Virol 71:8780-89) and Rabinowitz et al. (J Virol 76:791-801) and of Pitkow et al. (J Neurosci 21:7392-96) and GenBank AF063497. This claim is drawn to recombinant HSV-1 comprising a heterologous sequence of SEQ ID NO: 1. SEQ ID NO: 1 is a gene construct comprising (3' to 5') the 5 5' terminal nucleotides of an XbaI restriction site, and gene region for AAV2 rep, a gene region for AAV1 cap, and the 3' thymine of the XbaI site.

Conway teaches a method for the production of recombinant AAV2 vectors comprising the insertion into recombinant HSV-1 vectors genetic sequences encoding the AAV2 rep and cap proteins under the control of their native AAV promoters. Abstract. The reference teaches the insertion of the proteins by means of an XbaI restriction site. Page 8781 (section "Plasmids"). Because the reference teaches the insertion into an XbaI restriction site, it would have been obvious to those of ordinary skill in the art to create a construct comprising the same 3' and 5' XbaI terminals present in SEQ ID NO: 1. However, the reference does not teach the use of a construct comprising the rep sequence of AAV2 and a cap sequence of AAV1, or teach the specific AAV2 and AAV1 sequences present in SEQ ID NO: 1.

Rabinowitz teaches that AAV vectors may be cross packaged into AAV2 genomes through the substation of the AAV2 capsid sequence with that of another AAV genotype, such as AAV1. As this reference teaches that the capsid proteins of other AAV genotypes (including AAV1) may be used with the rep gene of AAV2 to produce hybrid AAV vectors, it would have been obvious to those of ordinary skill in the art that similar hybrid AAV particles could be produced by creating a construct comprising an AAV2 rep and an AAV1 cap sequence; and to substitute such a construct with the single genotype rep/cap constructs of Conway.

While the teachings of Rabinowitz also fail to specify the AAV2 and AAV1 sequences present in SEQ ID NO: 1, such sequences were known in the prior art. For example, Pitkow indicates that the pSSV9 AAV2 plasmid, from which the AAV2 sequence of SEQ ID NO: 1 was derived (see page 31 of the application) was known in the art. Page 7393 (section "AAV production"). The GenBank reference discloses an AAV1 genomic sequence sharing identity to residues 1717-4347 of SEQ ID NO: 1 (comprising the AAV1 cap gene region) at positions 1919-4549 of the disclosed sequence. It would therefore have been obvious to those of ordinary skill in the art to use these sequences in the making of the hybrid AAV constructs suggested by Conway and Rabinowitz for insertion into a recombinant HSV-1.

From these additional teachings it would have been obvious to those of ordinary skill in the art to substitute a region comprising the AAV1 cap gene region for a region comprising the homologous region of AAV2. Because the pSSV9 plasmid was a known source for such AAV2 constructs, it would have been obvious to those of ordinary skill in the art to have used this plasmid for such an insertion, and to use the known AAV1 sequence of the GenBank deposit as the source of the AAV1 sequence. One of the possible resulting sequences (after inclusion of the

XbaI terminal sequences) would be the sequence of SEQ ID NO: 1. Thus, the present claims describe a recombinant HSV-1 that would have been obvious to those of ordinary skill in the art.

14. **(New Rejection)** Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Conway, Rabinowitz, Pitkow, and GenBank AF063497 as applied to claim 1 above, and further in view of the teachings of Preston et al. (U.S. 2002/0028925). This claim is drawn to the recombinant HSV-1 of claim 1, wherein SEQ ID NO: 1 is inserted into a nonessential gene region of the HSV genome. It is noted that the Conway reference does not expressly indicate that the AAV sequence is inserted into such a region. However, Preston indicates that nonessential regions are useful for the insertion of foreign gene sequences into an HSV-1 genome. See e.g., pages 203. Thus, the additional teachings of this reference would have rendered the additional limitation of claim 3 obvious to those of ordinary skill in the art.

15. **(New Rejection)** Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Conway, Rabinowitz, Pitkow, and GenBank AF063497 as applied to claim 1 above, or Conway, Rabinowitz, Pitkow, GenBank AF063497, and Preston as applied to claim 3 above, and further in view of either of Mullaney et al. (J Gen Virol 70:449-54) or Herold (J Gen Virol 75:1211-22). This claim is directed to the HSV-1 of claim 1, wherein the heterologous sequence is inserted at the XbaI site of either UL2 or UL44.

The teachings of the previously applied references have been described above. While Conway teaches the use of an XbaI site for the insertion of a heterologous sequence into the HSV-1 genome, the reference does not specify the insertion into such a site in the UL2 or Ul44

gene regions. While Preston additionally indicates that such insertions may be made into UL2 or Ul44, the reference does not teach the presence of an XbaI site in these sequences.

Mullaney teaches the presence of an XbaI site, and that heterologous coding sequences may be inserted into this site, in the HSV-1 UL2 gene. See e.g., page 50. Herold notes the presence of such a site in the UL44 gene. Page 1214 (Figure 1(b)). From these teachings, with or without the additional identification of UL2 and UL44 as nonessential genes by Preston (page 2), it would have been obvious to those of ordinary skill in the art that these sites could be used for the insertion of AAV constructs suggested by the previously applied references. The combined teachings of the cited art therefore also render obvious the recombinant HSV-1 particles of claim 2.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

17. No claims are allowed.

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

U.S. 7,091,029. This reference also teaches the making of AAV vectors comprising the expression of AAV cap and rep from recombinant HSV-1. Claims. The reference indicates that the rep protein may be from AAV2 while the cap protein may be from another AAV, such as AAV1. Columns 15. The reference is considered to be duplicative to the Conway and/or Rabinowitz references above.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick J. Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachariah Lucas/
Primary Examiner, Art Unit 1648